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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,799	01/25/2006	Yasuhiro Kajihara	TAM-060	9645

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EXAMINER	
LAU, JONATHAN S	

ART UNIT	PAPER NUMBER
1623	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/565,799	KAJIHARA ET AL.	
	Examiner	Art Unit	
	Jonathan S. Lau	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *1-3* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is responsive to Applicant's Amendment and Remarks, filed 23 Oct 2008, in which claims 4, 5 and 7 are amended to change the scope and breadth of the claim and claim 4 is amended to be in independent form.

This application is the national stage entry of PCT/JP04/11036, filed 27 Jul 2004; and claims benefit of foreign priority document JAPAN 2003-202594, filed 28 Jul 2003. At present an English language translation of this foreign priority document is not of record.

Claims 1-8 are pending in the current application. Claims 1-3, drawn to non-elected inventions, are withdrawn.

Rejections Withdrawn

Applicant's Amendment, filed 23 Oct 2008, with respect to claims 4-8 rejected under 35 U.S.C. 112, second paragraph, as being indefinite has been fully considered and is persuasive, as amended claims 4, 5 and 7 do not recite derivative and recite definitely what compound is meant.

This rejection has been **withdrawn**.

The following new or modified grounds of rejection are necessitated by Applicant's Amendment, filed 23 Oct 2008, in which claims 4, 5 and 7 are amended to change the scope and breadth of the claim and claim 4 is amended to be in

independent form. Claims 6 and 8 depend from claims 4 and 7 respectively, and incorporate all limitations therein, including changes to the scope and breadth of the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Amended claims 4, 5 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rademacher et al. (US Patent 5,280,113, issued 18 Jan 1994, of record) in view of Wong et al. (Biochem J., 1994, 300, p843-850, provided by Applicant in IDS filed 06 Jul 2006).

Rademacher discloses glycoconjugates formed by the process of bonding to an N-haloacetylated glycosamine (column 5, lines 5-17). Rademacher discloses the process of forming a glycopeptide by conjugating the compound Galβ1-4GlcNAcβ1-2Manα1-6(Galβ1-4GlcNAcβ1-2Manα1-3)-Manβ1-4GlcNAcβ1-4GlcNAc (column 22, lines 55-65). Rademacher discloses the haloacetylated glycosylamines reacted with a thiol R'SH to form a thioether (spanning column 12, lines 35-65 and column 13, lines 1-10). The haloacetylation of the glycosamine of compound Galβ1-4GlcNAcβ1-2Manα1-6(Galβ1-4GlcNAcβ1-2Manα1-3)-Manβ1-4GlcNAcβ1-4GlcNAc gives the oligosaccharide of instant claim 4 in which R^1 is –NH-(CO)-$(CH_2)_1$-CH_2X and R^2 and R^3 are the formula (3) as defined in instant claim 4. Rademacher discloses the release of oligosaccharides from glycoproteins by chemical or enzymatic methods (column 1, lines 55-56).

Rademacher does not specifically disclose the formation of a glycopeptide by bonding said N-haloacetylated glycosamine to the thiol group of a peptide (instant claims 4 and 5). Rademacher does not specifically disclose the process for preparing a glycopeptide characterized by cleaving a saccharide of a glycopeptide from a peptide and subsequently bonding an aminated complex-type oligosaccharide derivative to the resulting peptide (instant claim 7).

Wong teaches the glycosylation of proteins using N-glycosyl haloacetamides site specific to a cysteine (abstract), or the thiol group of an amino acid in a peptide. Wong teaches the method of conjugating a defined oligosaccharide to cysteine side chains on a protein provides a finer-tuned strategy for synthetic glycosylation of proteins, and suggests the replacement of natural N-linked glycosylation sites with synthetic cysteine-

linked ones (page 849, left column, 2nd paragraph in Discussion section). Wong teaches this method allows one to obtain glycoproteins with homogeneous carbohydrate structures attached (page 849, left column, 2nd paragraph in Discussion section). Wong teaches cysteine-linked oligosaccharides mimic the natural N-linkage and can be released from neoglycoproteins, whereas there is no scheme for the release of unprotected sugars from neoglycoproteins (page 849, left column, 4th paragraph in Discussion section).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the invention of Rademacher with the teaching of Wong. Both Rademacher and Wong are drawn to the field of conjugating N-glycosyl haloacetamides to proteins. One of ordinary skill in the art would be motivated to combine Rademacher with the teaching of Wong because Wong teaches conjugating a defined oligosaccharide to cysteine side chains on a protein provides a finer-tuned strategy for synthetic glycosylation of proteins. One of ordinary skill in the art would have a reasonable expectation of success in combining Rademacher with the teaching of Wong because Rademacher discloses the haloacetylated glycosylamines reacted with a thiol R'SH to form a thioether, and a cysteine side chain is a thiol R'SH. Rademacher discloses the release of oligosaccharides from glycoproteins by chemical or enzymatic methods. Wong teaches the replacement of sites of natural glycosylation with synthetic cysteine-linked ones.

It would have been obvious to one of ordinary skill in the art to cleave a saccharide of a glycopeptide from an amino acid and subsequently bond an aminated

complex-type oligosaccharide to the resulting peptide. One would have been motivated to combine Rademacher in view of Wong to replace oligosaccharides from glycoproteins with said aminated complex-type oligosaccharide because Wong teaches this allows one to obtain glycoproteins with homogeneous carbohydrate structures attached and that cysteine-linked oligosaccharides mimic the natural N-linkage and can be released from neoglycoproteins.

Response to Applicant's Remarks:

Applicant's Remarks, filed 23 Oct 2008, have been fully considered and found not to be persuasive.

Applicant notes that the glycopeptides of the instant invention is superior to the aparagine-linked glycopeptides in resistance to hydrolysis and uniform in physiological activity. However, one of ordinary skill in the art would expect these properties to be present based on the teachings of the prior art. Wong at page 845, right column, last 10 lines of partial paragraph 1, details that release of the oligosaccharide from the neoglycoprotein was effected by hydrazinolysis rather than simple hydrolysis, providing guidance to one of ordinary skill in the art that hydrolysis of the thiol-linked oligosaccharide would require harsher conditions leading to the degradation of the oligosaccharide. Wong teaches this method allows one to obtain glycoproteins with homogeneous carbohydrate structures attached (page 849, left column, 2nd paragraph in Discussion section), which provides guidance for one of ordinary skill in the art to reasonably expect uniform activity based in the homogeneity of the carbohydrate structures attached to the protein.

Amended claims 6 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rademacher et al. (US Patent 5,280,113, issued 18 Jan 1994, cited in PTO-892) in view of Wong et al. (Biochem J., 1994, 300, p843-850, provided by Applicant in IDS filed 06 Jul 2006) as applied to claims 4, 5 and 7 above, and further in view of Wright et al. (Trends in Biotechnology, 1997, 15, p26-32, of record).

Rademacher in view of Wong renders obvious as above.

Rademacher in view of Wong does not specifically teach the peptide being an antibody (instant claims 6 and 8).

Wright teaches all antibodies are glycosylated at conserved positions and the presence of carbohydrate can be critical (abstract). Wright teaches antibodies are glycosylated with a Galβ1-4GlcNAcβ1-2Manα1-6(Galβ1-4GlcNAcβ1-2Manα1-3)-Manβ1-4GlcNAcβ1-4(Fuc)-GlcNAc oligosaccharide (page 28, figure 2 at top of page, structure 4).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine Rademacher in view of Wong with the teaching of Wright of the peptide being an antibody. Rademacher, Wong and Wright are all drawn to the field of glycosylation of peptides. One of skill in the art would be motivated to combine Rademacher in view of Wong with the teaching of Wright because Wright teaches all antibodies are glycosylated at conserved positions and the presence of carbohydrate can be critical. One of ordinary skill in the art would have reasonable expectation of success in combining Rademacher in view of Wong with the teaching of Wright because

Wright teaches antibodies are glycosylated with an oligosaccharide Galβ1-4GlcNAcβ1-2Manα1-6(Galβ1-4GlcNAcβ1-2Manα1-3)-Manβ1-4GlcNAcβ1-4(Fuc)-GlcNAc which is similar in structure to the oligosaccharide taught by Rademacher Galβ1-4GlcNAcβ1-2Manα1-6(Galβ1-4GlcNAcβ1-2Manα1-3)-Manβ1-4GlcNAcβ1-4GlcNAc.

Response to Applicant's Remarks:

Applicant's Remarks, filed 23 Oct 2008, have been fully considered and found not to be persuasive.

Applicant's Remarks with regard to Rademacher in view of Wong are addressed as above.

Applicant notes that Wright is teaches the glycosylation of antibodies. It is well known in the art that antibodies are gamma globulin proteins and taught in Wright to be glycosylated. Therefore antibodies are a subgenus of proteins, which are in turn a subgenus of peptides, and similarly a glycosylated antibody is subgenus of glycopeptides. Applicant notes that Wright does not teach the oligosaccharide bonded by a thiol group, however the combined teaching of Rademacher in view of Wong and further in view of Wright is relied upon to teach the oligosaccharide bonded by a thiol group to an antibody.

Conclusion

No claim is found to be allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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